

WHAT IS CLAIMED IS:

5        1. A method for differentiating DNA species originating from different individuals in a biological sample comprising the step of determining epigenetic differences between these DNA species.

10      2. A method according to claim 1 wherein the epigenetic difference is a difference in DNA methylation.

15      3. A method according to claim 1 wherein the biological sample is plasma or serum.

20      4. A method according to claim 1 wherein the biological sample is blood.

25      5. A method according to claim 1 wherein one of the individuals is a pregnant female and the other individual is an unborn fetus.

30      6. A method according to claim 1 wherein one of the individuals is a transplantation recipient and the other individual is an organ donor.

25      7. A method according to claim 6 wherein the transplantation is a bone marrow transplantation.

30      8. A method according to claim 1 further comprising the step of measuring concentrations of DNA species having an epigenetic difference.

25      9. A method according to claim 2 wherein the epigenetic difference is a DNA methylation difference.

30      10. A method according to claim 2 further comprising the step of adding sodium bisulfite to the biological sample or to the DNA species to detect a DNA methylation difference.

11. A method according to claim 2 further comprising the step of performing a methylation-specific polymerase chain reaction to detect a DNA methylation difference.
- 5           12. A method according to claim 10 further comprising the step of sequencing DNA to detect a DNA methylation difference.
- 10           13. A method according to claim 10 further comprising the step of performing primer extension to detect a DNA methylation difference.
14. A method according to claim 5 wherein the biological sample is maternal plasma or serum.
- 15           15. A method according to claim 14 further comprising the step of measuring the concentration of fetal DNA in maternal plasma or serum.
16. A method according to claim 15 wherein the concentration of fetal DNA measured is used to predict, monitor or diagnose or prognosticate a disorder.
- 20           17. A method according to claim 15 wherein an epigenetic mark is associated with a fetal or maternal disorder.
18. A method according to claim 17 wherein the disorder is a chromosomal aneuploidy.
- 25           19. A method according to claim 18 wherein the chromosomal aneuploidy is trisomy 21 (Down syndrome).
20. A method according to claim 17 wherein the disorder is preeclampsia.
- 30           21. A method according to claim 17 wherein the disorder is an imprinting disorder.

22. A method according to claim 21 wherein the disorder is Prader-Willi syndrome.

23. A method according to claim 21 wherein the disorder is Angelman syndrome.

5

24. A method according to claim 14 wherein an epigenetic difference in fetal cells in the placenta is used as a fetus-specific marker in maternal plasma or serum.

10 25. A method according to claim 6 further comprising the step of measuring the concentrations of donor and recipient DNA.

26. A method according to claim 25 wherein the measurements are used to predict the clinical progress of the transplantation recipient.

15 27. A method according to claim 1 wherein one individual is male and the other individual is female.

28. A method according to claim 27 wherein the epigenetic marker is an inactivated X chromosome of the female individual.

20 29. A method according to claim 28 wherein methylated DNA sequences on the inactivated X chromosome are used to detect DNA originating from the female individual.

25 30. A method according to claim 1 wherein the epigenetic differences are analyzed inside cells.

31. A method according to claim 30 wherein the epigenetic differences are analyzed using in-situ methylation-specific polymerase chain reaction.

30 32. A method according to claim 1 wherein the epigenetic differences are used to sort or isolate cells from the individuals.

33. A method according to claim 1 wherein the epigenetic differences are used to purify DNA from the individuals.

34. A kit for differentiating DNA species originating from different individuals in a biological sample comprising one or more reagents for ascertaining the methylation status of a species of DNA.

35. A kit according to claim 34 wherein the reagent for ascertaining the methylation status of the maternal DNA is sodium bisulfite.

36. A kit according to claim 34 further comprising one or more reagents for detecting the presence of DNA.

37. A kit according to claim 34 further comprising one or more reagents for amplifying the amount of DNA present in the biological sample.

38. A kit according to claim 34 further comprising one or more apparatuses for obtaining a DNA sample.